

इंटरनेट

मानक

Disclosure to Promote the Right To Information

Whereas the Parliament of India has set out to provide a practical regime of right to information for citizens to secure access to information under the control of public authorities, in order to promote transparency and accountability in the working of every public authority, and whereas the attached publication of the Bureau of Indian Standards is of particular interest to the public, particularly disadvantaged communities and those engaged in the pursuit of education and knowledge, the attached public safety standard is made available to promote the timely dissemination of this information in an accurate manner to the public.

“जानने का अधिकार, जीने का अधिकार”

Mazdoor Kisan Shakti Sangathan

“The Right to Information, The Right to Live”

“पुराने को छोड़ नये के तरफ”

Jawaharlal Nehru

“Step Out From the Old to the New”

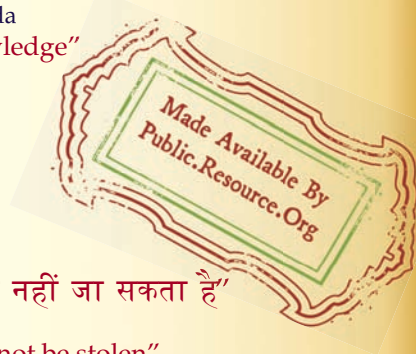
IS 12572-3 (1988): Guide for evaluation of medical devices for biological hazards, Part 3: Method of testing by tissue implantation [MHD 12: Hospital Equipment]



“ज्ञान से एक नये भारत का निर्माण”

Satyanarayan Gangaram Pitroda

“Invent a New India Using Knowledge”



“ज्ञान एक ऐसा खजाना है जो कभी चुराया नहीं जा सकता है”

Bhartrhari—Nitiśatakam

“Knowledge is such a treasure which cannot be stolen”

BLANK PAGE



Indian Standard

GUIDE FOR EVALUATION OF MEDICAL
DEVICES FOR BIOLOGICAL HAZARDS

PART 3 METHOD OF TESTING BY TISSUE IMPLANTATION

भारतीय मानक

जैव-वैज्ञानिक खतरों के लिए चिकित्सीय युक्तियों के मूल्यांकन की मार्गदर्शिका
भाग 3 ऊतक-प्रत्यारोपण द्वारा परीक्षण की पद्धतियाँ

UDC 615.4: 614.8 : 616-002 : 616-089-843

DESCRIPTORS : MEDICAL DEVICES, BIOLOGICAL HAZARDS
TISSUE IMPLANTATION

© BIS 1989

BUREAU OF INDIAN STANDARDS
MANAK BHAVAN, 9 BAHADUR SHAH ZAFAR MARG
NEW DELHI 110002

FOREWORD

This Indian Standard (Part 3) was adopted by the Bureau of Indian Standards on 14 September 1988, after the draft finalized by the Medical Glass Instruments and Appliances Sectional Committee had been approved by the Consumer Products and Medical Instruments Division Council.

This part (Part 3) is one of a series of methods of test for assessing the biological hazards of medical devices that directly come in contact with body tissues or substances that are to be introduced into the body by means other than oral.

Part 2 of this standard provides **guidance** on the selection of recommended methods of test for the assessment of biological hazards in medical devices which has been referred to in this part.

This standard is proposed to be published in 12 parts. Other parts are as follows:

Part 1 Terminology

Part 2 Selection of biological methods of test

Part 4 Method of test for systemic toxicity : Assessment of acute toxicity of extracts from medical devices

Part 5 Method of test for intracutaneous reactivity of extracts from medical devices

Part 6 Method of test for systemic toxicity : Assessment of pyrogenicity in rabbits of extracts from medical devices

Part 7 Methods of test for sensitization : Assessment of potential of medical devices to produce delayed contact dermatitis

Part 8 Method of test for skin irritation of extracts from medical devices

Part 9 Method of test for skin irritation of solid medical devices

Part 10 Method of test for dental materials

Part 11 Method of test for eye irritation

Part 12 Methods of test for toxicity to cells in culture of extracts from medical devices

In the preparation of this standard, assistance has been derived from BS 5736 : Part 2 : 1981 'Evaluation of medical devices for biological hazards: Part 2 Methods of testing by tissue implantation', issued by the British Standards Institution, UK.

Indian Standard

GUIDE FOR EVALUATION OF MEDICAL DEVICES FOR BIOLOGICAL HAZARDS

PART 3 METHOD OF TESTING BY TISSUE IMPLANTATION

I SCOPE

1.1 This standard (Part 3) describes a method of test designed to provide information on the effects of direct contact of a test material with living tissue when implanted into the paravertebral muscle of the rabbit for a period of 7 days.

1.2 This method of test is recommended in the initial assessment of devices in category A and C (*see* Part 2 of this standard) :

- a) *Category A* — Those intended for long-term (long-term covers a period from a few months to permanent use) implantation within the body tissue, for example, artery grafts and hip prostheses; and
- b) *Category C* — Those intended for short-term (short-term covers a period from a few minutes to several weeks continuous use) use within the body or in contact with mucosal surfaces, for example, tracheal tubes, urinary catheters and intravenous cannulae.

2 DEFINITIONS

For the purpose of this standard, the following definitions shall apply.

2.1 Final Product

The medical devices in its ready-for-use state.

2.2 Implant

The test specimen, positive control specimen or negative control specimen (*see* 2.8, 2.5 and 2.6) that has been implanted.

2.3 Implant Site

The implant and 5 mm tissue surrounding it, measured from the centre of the implant.

2.4 Medical Device

Any item used in medical treatment, diagnosis or contraception, not intended to have a pharmacological action on the body.

2.5 Negative Control Specimen

A piece of material which, when implanted by the procedure described in 5, produces a negative reaction (*see* 7.3).

NOTE — Additive-free polyethylene is suitable.

2.6 Positive Control Specimen

A piece of material which, when implanted by the procedure described in 5 produces a positive reaction (*see* 7.4).

NOTE — Tin stabilized polyvinylchloride is suitable.

2.7 Test Material

The final product or sample of final product that is to be tested.

2.8 Test Specimen

The piece of test material that is implanted.

3 ANIMALS AND HUSBANDRY

3.1 Not fewer than three rabbits of white strain, preferably Newzeal and type, shall be used. They shall be healthy adults whose paravertebral muscles are sufficiently large in size to allow for implantation of test and control specimens as described in 5.2.

3.2 The animals shall be housed individually and shall have free access to food and water.

4 TEST AND CONTROL SPECIMENS

4.1 Number of Specimens Required

The minimum number of specimens for Implantation in each rabbit in accordance with 5 shall be:

- a) not fewer than two positive control specimens,
- b) not fewer than two negative control specimens, and
- c) not fewer than four test specimens.

NOTE — It may be necessary to implant more specimens than the minimum required because of loss, for example, by extrusion, of implants during the 7 day test period.

4.2 Sterilization and Handling of Specimens

4.2.1 The specimens from pre-sterilized devices and the pre-sterilized controls shall be aseptically handled.

4.2.2 All other test specimens shall be sterilized by autoclaving and thereafter shall be aseptically handled.

4.3 Preparation of Specimens

Immediately before implanting, cut or shape the test materials and, if necessary, the controls, into specimens nominally 10 x 1 x 1 mm with smooth sides to minimize mechanical trauma during implantation.

4.3.1 Place each specimen in a sterile solution containing 9 g/l sodium chloride.

5. TEST PROCEDURE

5.1 Preparation of Animals

5.1.1 Anaesthetize the rabbits by injection, for example, with 30 mg/kg pentobarbitone sodium intravenously, and record the anaesthetic and the route of administration used.

5.1.2 Clip the fur on the back of the rabbits close to the skin and swab the clipped area with anti-septic solution.

5.2 Implantation of Specimens

5.2.1 Implant in one of the rabbits, the appropriate number of test and control specimens in the positions shown in Fig. 1. using the procedure described in 5.2.3 to 5.2.7.

5.2.2 Each implant shall be at least 10 mm from any other implant and the positive control

specimen shall be at least 30 mm to the rear of other implants.

5.2.3 Aseptically place a specimen into a sterile needle (hypodermic type) of cannular length 19 to 35 mm and of a bore such that the specimen is a snug but not tight fit, for example, 1.8 mm bore.

5.2.4 Insert a sterile stylet behind the specimen in the needle.

5.2.5 Insert the needle vertically into the paravertebral muscle of the rabbit.

5.2.6 Hold the stylet in place whilst the needle is gently withdrawn leaving the stylet in place.

5.2.7 When the needle is free from the skin, withdraw the stylet likewise, leaving the specimen implanted within the muscle.

5.2.8 Repeat the implantations in two further rabbits.

5.3 Recovery of Implant Sites

5.3.1 After the implants have been in position for 7 days, kill the rabbits with an overdose of anaesthetic and place them in the prone position with the legs splayed.

5.3.2 Carefully excise the implant sites, leaving the implants in position,

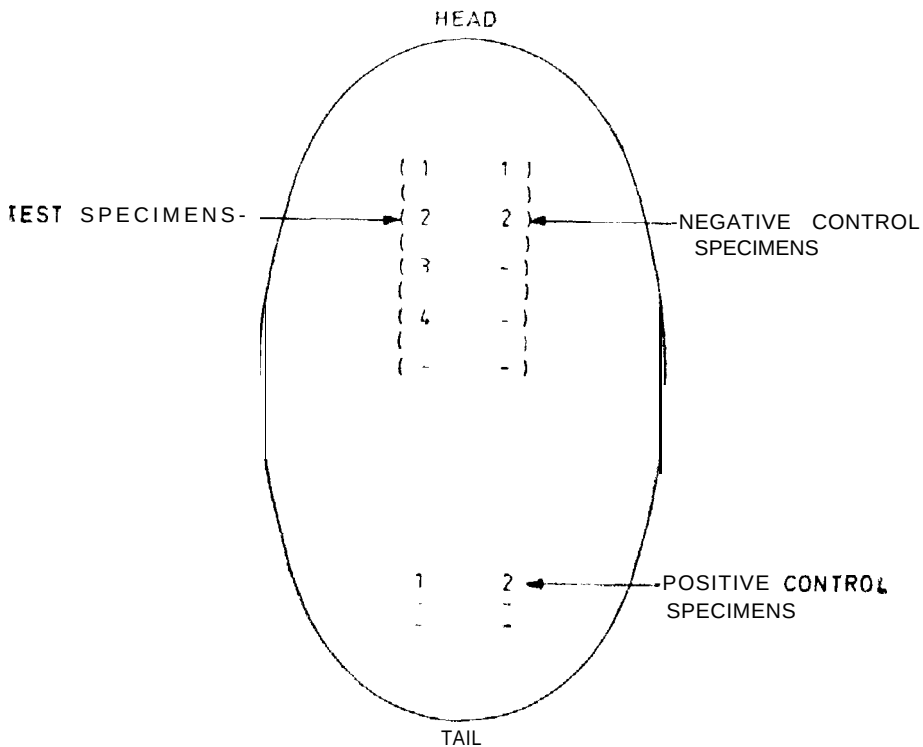


FIG. 1 ARRANGEMENT OF IMPLANTS IN A SINGLE RABBIT

5.4 Examination of Implant Sites

5.4.1 Microscopic Examination

5.4.1.1 Examine each excised implant site under normal vision or with the aid of a low magnification lens. Record the nature, extent and distribution of any tissue reaction observed.

5.4.1.2 If any negative or positive control specimen evokes a reaction other than that described in 7.3 and 7.4 respectively, the results of the test specimens in that rabbit shall be rejected and the test repeated in a further rabbit.

5.4.1.3 If any test specimen implant site shows a positive reaction (see 7.4), at least one of these sites shall be selected for histological examination (see 5.4.2) to confirm the response.

5.4.1.4 If any test specimen implant sites shows a negative reaction (see 7.3), all the test specimen implant sites and the negative control implant sites shall be recovered for histological examination to confirm the response.

5.4.2 Histological Examination

5.4.2.1 Preserve the excised implant sites specified in 5.4.1 in formal saline.

5.4.2.2 Prepare sections transverse to the excised implant sites.

NOTE- Ideally, the implant should remain in place during preparation for sectioning to ensure correct orientation of the surrounding tissue unless adverse reaction with dehydrating or defatting solvents is likely to occur. Hard implants may be removed before cutting of sections, if cutting would otherwise be difficult.

5.4.2.3 Stain the sections with haematoxylin and eosin.

5.4.2.4 Examine the histological sections microscopically and record the findings.

6. PRESENTATION OF RESULTS

6.1 The results shall be submitted in a test report that includes a complete record of the procedures and any other relevant data used in the assessment of results as described in 7.

6.2 If more than the minimum number of test specimens or control specimens are recovered (see 4.1), all recovered specimens shall be considered as part of the test.

7. ASSESSMENT OF RESULTS

7.1 The assessment of results should be carried out by a toxicologist who is aware of the conditions of use for the final product and has appropriate chemical and biological data concerning it [see 3.3 and 3.4 of IS 12572 (Part 2) : 1988].

7.2 The overall assessment of the test results shall be carried out by taking into consideration all information in the test report.

7.3 A reaction shall be considered a negative reaction if there is no reaction or if there is a reaction that can be attributed to experimental trauma, typically asymmetrical, non-necrotic and non-inflammatory,

7.4 A reaction shall be considered a positive reaction if there is a toxic reaction, typically with necrosis and inflammation symmetrically around the implant.

7.5 A test material shall have evoked a positive response if any test specimen obtained from it evokes a positive reaction.

7.6 The results of the assessment shall be recorded in the test report.

Standard Mark

The use of the Standard Mark is governed by the provisions of the **Bureau of Indian Standards Act, 1986** and the Rules and Regulations made thereunder. The Standard Mark on products covered by an Indian Standard conveys the assurance that they have been produced to comply with the requirements of that standard under a well defined system of inspection, testing and quality control which is devised and supervised by BIS and operated by the producer. Standard marked products are also continuously checked by BIS for conformity to that standard as a further safeguard. Details **of conditions** under which a licence for the use of the Standard Mark may be granted to manufacturers or producers may be obtained from the Bureau of Indian Standards.

Bureau of Indian Standards

BIS is a statutory institution established under the *Bureau of Indian Standards Act, 1986* to promote harmonious development of the activities of standardization, marking and quality certification of goods and attending to connected matters in the country.

Copyright

BIS has the copyright of all its publications. No part of these publications may be reproduced in any form without the prior permission in writing of **BIS**. This does not preclude the free use, in the course of implementing the standard, of necessary details, such as symbols and sizes, type or grade designations. Enquiries relating to copyright be addressed to the Director (Publications), **BIS**.

Revision of Indian Standards

Indian Standards are reviewed periodically and revised, when necessary and amendments, if any, are issued from time to time. Users of Indian Standards should ascertain that they are in possession of the latest amendments or edition. Comments on this Indian Standard may be sent to **BIS** giving the following reference:

Doc : No. CPDC 12 (1928)

Amendments Issued Since Publication

Amend No.	Date of Issue	Text Affected

BUREAU OF INDIAN STANDARDS

Headquarters :

Manak Bhavan, 9 Bahadur Shah Zafar Marg, New Delhi 110002
Telephones : 331 01 31, 331 13 75

Telegrams : Manaksanstha
(Common to all Offices)

Regional Offices:

Telephone

Central: Manak Bhavan, 9 Bahadur Shah Zafar Marg
NEW DELHI 110002

{ 331 01 31
331 13 75

Eastern : 1/14 C. I. T. Scheme VII M, V. I. P. Road, Maniktola
CALCUTTA 700054

36 24 99

Northern : SCO 445-446, Sector 35-C, CHANDIGARH 160036

{ 2 18 43
3 16 41

Southern : C. I. T. Campus, IV Cross Road, MADRAS 600113

{ 41 24 42
41 25 19
41 29 16

Western : Manakalaya, E9 MIDC, Marol, Andheri (East)
MUMBAI 400093

6 32 92 95

Branches: AHMADABAD, BANGALORE, BHOPAL, BHUBANESHWAR,
GUWAHATI, HYDERABAD, JAIPUR, KANPUR, PATNA,
TRIVANDRUM